IN THE SPECIFICATION:

Please amend the paragraph extending from line 18 to line 20 of page 9 to read as follows:

Figures 1A-1D are top plan views illustrating ~~Figure 1 illustrates~~ various designs of delivery devices according to the invention which are in the form of a tube open at one or both ends, and having one or two holes that allow for diffusion of encapsulated therapeutic agent, e.g., virus.

Please amend the paragraph extending from line 1 to line 2 of page 10 to read as follows:

Figure 2 is a top plan view illustrating ~~illustrates~~ a block containing small holes for storage of drug delivery devices according to the invention.

Please amend the paragraph extending from line 3 to line 5 of page 10 to read as follows:

Figures 3A-3C are top plan, side and sectional views, respectively, illustrating ~~Figure 3 illustrates~~ a tube for use in the invention having a length of 0.197 inch, wall thickness of 0.0035 inch, diameter of 0.041 inch, and round hole having a diameter of 0.020 inch.

Please amend the paragraph extending from line 6 to line 8 of page 10 to read as follows:

Figures 4A-4C are top plan, side and sectional views, respectively, illustrating ~~Figure 4 illustrates~~ another tube design having a length of 0.197 inch, a wall thickness of 0.0035 inch, a diameter of 0.41 inch, and two round holes having a diameter of 0.020 inch.

Please amend the paragraph extending from line 9 to line 14 of page 10 to read as follows:

Figures 5A-5C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 5 illustrates~~ a different tubular bottle-like design having a length of 0.197 inch, which is of comprised of two sections of differing diameter, wherein the larger diameter portion (0.041 inch in diameter) comprises a hole (0.020 inch in diameter) allowing for diffusion of

encapsulated active agent, and tapers into a smaller diameter portion (diameter of 0.02 inch), and wherein the wall thickness of both portions is 0.0035 inch.

Please amend the paragraph extending from line 15 to line 17 of page 10 to read as follows:

Figures 6A-6C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 6 illustrates~~ another tubular design having a length of 0.197 inch, a wall thickness of 0.0035 inch, a hole allowing for diffusion which is 0.020 inch in diameter, and having a tube diameter of 0.041 inch.

Please amend the paragraph extending from line 18 to line 18 of page 10 to read as follows:

Figures 7A-7C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 7 illustrates~~ another tubular design (bottle-like configuration) having an overall length of 0.197 inch, a wall thickness of 0.0035 inch, and a diameter of 0.041 inch (larger diameter portion), with a rectangular opening of 0.039 inches in length.

Please amend the paragraph extending from line 1 to line 3 of page 11 to read as follows:

Figures 8A-8C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 8 illustrates~~ another tube design having an overall length of 0.197 inch, a wall thickness of 0.0035 inch, a diameter of 0.041 inch, and a rectangular opening 0.118 inches in length.

Please amend the paragraph extending from line 4 to line 6 of page 11 to read as follows:

Figures 9A-9C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 9 depicts~~ yet another tube design having a length of 0.197 inch, wall thickness of 0.035 inch, diameter of 0.041 inch, and a rectangular opening 0.197 inches in length.

Please amend the paragraph extending from line 7 to line 9 of page 11 to read as follows:

Figures 10A-10C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 10 depicts~~ another tubular design having a length of 0.197 inch, a diameter of 0.41 inch (overall), wall thickness of 0.035 inch, and two rectangular holes 0.039 inch in length.

Please amend the paragraph extending from line 10 to line 12 of page 11 to read as follows:

Figures 11A-11C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 11 depicts~~ another bottle-like tubular designs having an overall length of 0.197 inch, diameter of 0.041 inch (large portion), wall thickness of 0.035 inch, rectangular opening that is 0.039 inch long and a circular opening 0.020 inch in diameter.

Please amend the paragraph extending from line 13 to line 15 of page 11 to read as follows:

Figures 12A-12C are top plan, bottom, and sectional views, respectively, illustrating ~~Figure 12 depicts~~ another bottle-like tubular design having an overall length of 0.197 inch, a diameter of 0.041 inch, wall thickness of 0.035 inch, and two round holes that are 0.020 inch in diameter.

After line 15, on page 11 insert the following header:

--Detailed Description--

Please amend the paragraph extending from line 16 on page 11 to line 4 on page 12 to read as follows:

Seeds with different types of perforations allow drugs to be released at different rates, e.g., rectangular holes can be used to release chemotherapeutic drugs to be released intratumorally at a fast rate. Spherical/circular holes can be used to deliver biologics at a relatively slow rate at the tumor site. The subject seeds, which are alternatively referred to as "~~GENESEEDS®~~ GENESEED® pharmaceutical delivery devices", can also be filled with a cocktail of drugs containing genetic drugs (viruses, plasmids, etc.), chemotherapeutic drugs, radionuclides, toxins, cytokines, therapeutic enzymes, antibiotics, antibodies, and conjugates/combinations thereof, etc. The tubes preferably will be made of stainless steel,

gold, titanium, platinum, or other biocompatible metals or an alloy of metals. The tubes can also be made of a suitable biocompatible polymeric material.

Please amend the paragraph extending from line 16 on page 17 to line 10 on page 18 to read as follows:

The prototype ~~GENESEED®~~ GENESEED® pharmaceutical delivery device consists of a metallic tube made of high purity titanium metal suitable for medical applications with a thickness of 0.005 inch. Low weight, high strength titanium is the metal of choice for the majority of implantable devices. Titanium grade metal specified in the American Society for Testing of Materials F67-69 "Standard Specifications for Unalloyed Ti for Surgical Implant Applications" will be used. Titanium of the same grade has been in use in surgical implants for interstitial treatment of cancer. Please refer to registry of sealed sources and device document number: NR-460-S-165-S, NR-460-S-160-S and GA-645-5101 -S. The tube will be either closed on one end or both ends may be open. The titanium tube will contain one or two holes of diameter 0.5 mm (see Figure 1). We will investigate the different designs in order to determine the optimum seed configuration for gene delivery. The different designs that we have considered include the following:

a. titanium tube with one end open, with two holes of diameter 0.5 mm
b. titanium tube with both ends open, with two holes of diameter 0.5mm
c. titanium tube with one end open, with one hole of diameter 0.5mm
d. titanium tube with both ends open, with one hole of diameter 0.5mm

Please amend the paragraph extending from line 4 to line 9 of page 19 to read as follows:

~~GENESEEDS®~~ GENESEED® pharmaceutical delivery devices will function as delivery devices to freeze the biological material and transfer it to the hospital in the frozen state until ready for use in patients. If needed, the ~~GeneSeeds~~ delivery devices can be placed in specially fabricated metallic cartridges and kept at very low temperatures. Seed cartridges for storage of radioactive seeds are already available in the brachytherapy industry and these cartridges can be modified for low temperature applications.

Please amend the paragraph extending from line 11 on page 19 to line 5 on page 20 to read as follows:

High purity titanium tubes (medical grade metal) are cut to required size (± 3%). The seeds will then be washed with an aqueous solution containing a mild detergent followed by acetone and sterile water for injection. The washed seeds will be dried in an oven at 110°C for about two hours. Autoclaving will be performed to assure sterility. The seeds will be allowed to cool to room temperature. The viral solution will be added to the seed, using specially designed transfer devices which are adaptable to robotic control. The transfer device containing ~~GENESEEDS®~~ GENESEED® pharmaceutical delivery devices will be kept frozen at -70 °C until ready for use in animals. Small numbers of seeds can be prepared manually for initial preclinical studies. Once a suitable configuration is identified, large scale manufacturing of GeneSeeds can be performed employing the proprietary technology developed by Best Industries Inc. and is currently in use for the production of iodine and palladium brachytherapy seeds, Suthanthiran K., Device and method for encapsulating radioactive materials, U.S. Patent No. 4,891,165, January 2, 1990. This method employs an automated dispensing device to add drug to seeds. It is oft particular interest that much of the currently available radioactive seed implant technology will be directly adaptable for use with ~~"GeneSeeds"~~ devices according to the present invention.

Please amend the paragraph extending from line 13 to line 19 of page 23 to read as follows:

The four different types of ~~GENESEEDS®~~ GENESEED® pharmaceutical delivery devices described in Figure 1 will be filled with viral solutions and frozen at -70°C. The seeds will be implanted interstitially in mice bearing tumor xenografts (prostate tumor models). Melting and release of viral solution occurs rapidly. At selected time points post implantation, the animals will be sacrificed and the tumor will be excised. The extent of diffusion and virus entry into tumor cells will be evaluated using histochemistry. The optimum design) will slowly diffuse the viral material, allowing maximal intracellular viral uptake in tumor cells.

Please amend the title on lines 5 to 6 of page 25 to read as follows:

Evaluation of viral distribution within tumors as a function of time after ~~GENESEED®~~ GENESEED® pharmaceutical delivery devices implant

Please amend the paragraph extending from line 20 on page 26 to line 5 on page 27 to read as follows:

We anticipate tumor growth delay to occur in GENESEED® pharmaceutical delivery devices and direct intra-tumor injected animals. If needed, additional experiments will be performed using more than one seed per tumor. The observation of tumor growth delay comparable to direct tumor injection will be the endpoint confirming the utility of GENESEED® pharmaceutical delivery devices for viral vector delivery. Improved distribution experiments to show GENESEED® pharmaceutical delivery device superiority over direct injection may require larger tumors in a large tumor model system and may be considered in a Phase II proposal.